

REMARKS

In the outstanding Office Action, claims 1-28 and 31-32 were presented for examination. Claims 1-28 and 31-32 stand provisionally rejected for double patenting under 35 USC §103 over claims 1-20 of copending application number 10/469,747. Claims 1-7, 9-14, 18-22, 24-27 and 31-32 were again rejected under USC §112 first paragraph as failing to comply with the written description requirement, notwithstanding applicant's remarks to the contrary.

The Office Action has been most carefully studied. In this amendment, claims 1, 2, 9, 10 and 13 have been amended. New claim 33 has been added. Accordingly, as will be discussed in detail below, it is believed that the application is clearly in condition for allowance.

Withdrawal of Rejections

The withdrawal of the rejections of a number of claims for indefiniteness and of unpatentability rejections based on Chang et al. and Olsen et al. are appreciated.

Information disclosure statement

The information disclosure statement filed December 22, 2005 is refiled herewith accompanied by a complete copy of the reference to Purtell et al. It is regretted that the copies previously furnished to the Office were made from only one of the sides of a double-sided document.

Claim Amendments

Independent claims 1, 2, 9 and 10 have been amended, to define the recited protein or protein monomer as comprising at least one stretch of at least 10 consecutive

Gly-Xaa-Yaa triplets, wherein at least 5% of the total number of protein amino acid residues are proline residues in order to limit the claims to be commensurate with applicant's arguments in the amendment filed 27 October 2005, with a view to expediting allowance of same.

In addition, claims 9 and 10 have been amended to recite a process step of dissolving the protein or protein monomer in saline, making explicit subject matter that was inherent in the respective claim before amendment. Support for the language used may be found in the specification, for example at page 13, lines 10-11.

Claim 13 has been amended to remove the typographical error kindly pointed out by the Office.

New claim 33 is directed to the subject matter of claim 1, essentially as written prior to this amendment.

Double Patenting

In reply to the double patenting rejection set forth in the Office action of June 24, 2005 applicant provided a cogent explanation of why the claims of the present application are patentably distinct from the claims of copending application number 10/469,747. The Office has tacitly acknowledged this distinction in the outstanding action by relying upon the reference disclosure, citing paragraphs [0030] and [0067], rather than its claims, in dismissing applicant's arguments as not persuasive.

When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. See *General Foods Corp. v.*

Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). The Office relies upon the disclosure of 10/469,747 to support its continued double patenting rejection. This is clearly improper. Accordingly, it is respectfully requested that the double patenting rejection be reconsidered once again and be withdrawn.

Claim Rejections - 35 U.S.C. §112, First Paragraph, Written Description

Claims 1-7, 9-14, 18-22, 24-27 and 31-32 are again rejected as failing to comply with the written description requirement, notwithstanding applicant's arguments to the contrary. The Office considered those arguments unpersuasive because "the feature on which applicant relies (i.e. a recombinant gelatin-like protein comprising Gly-Xaa-Ybb triplets) is not found in the rejected claims. Independent claims 1, 2, 9 and 10 and, by virtue of their dependencies, claims 3-7, 11-14, 24-27 and 31-32 now require that the protein or protein monomer defined in the respective claim comprise at least one stretch of at least 10 consecutive Gly-Xaa-Yaa triplets, wherein at least 5% of the total number of protein amino acid residues are proline residues. Accordingly, the Office's basis for rejection is removed and claims 1-7, 9-14, 18-22, 24-27 and 31-32 clearly meet the written description requirement, for the reasons set forth in the response filed October 27, 2005, and are therefore allowable, for this reason alone.

Furthermore, the examples clearly and sufficiently disclose the genus defined in claims 1-7, 9-14, 18-22, 24-27 and 31-32, as now amended, since the examples show both a variation in IEP and in molecular weight while retaining the general requirements of a gelatin-like protein.

Clearly the Office's remarks on page 6 of the outstanding action, that the term recombinant gelatin means:

"any amino acid sequence that would retain a molecular weight of at least 10-50 kDa, and that has an IEP of less than 8"

and on page 9 that:

" The claims are drawn to any recombinant gelatin like protein that encompasses any amino acid that may be altered as long as the peptide retains the claimed molecular weight and an isoelectric point below 8. The possible variations are enormous."

are not remotely relevant to the amended claims.

In addition, applicant respectfully submits, for the record that the remarks accompanying the Amendment filed October 27, 2005, to the effect that:

"Any amino acid may be altered as long as the peptide retains the claimed molecular weight of the monomer and an isoelectric point below 8"

was taken out of context by the Office. This statement was used to argue that applicant claimed any polypeptide having the 'right' molecular weight and IEP, but that argument clearly ignores the term 'gelatin-like'. In relation to the claims as now amended, "Any amino acid" can be understood to refer to those amino acids that a person skilled in the art might modify, without affecting colloid osmotic function, to obtain the desired isoelectric point. Examples are the aspartic acid/asparagine and glutamic acid/glutamine replacements set forth in claim 7.

Further specific disclosures of possible amino acid variations are set forth in the specification at page 10, lines 14-16:

"Yet further the isoelectric point (IEP) and number of amino acids with an ionizable residual group can be tuned by the composition of acidic and basic amino acid residues in gelatin-like proteins.";

on page 10 at lines 18-26:

"Recombinant gelatin-like proteins according to the invention have an isoelectric point of less than 8. At pH 8 lysine and arginine are positive charged, glutaminic acid and asparaginic acid are negative charged and glutamine and asparagine are neutral. Glutamine and asparagine can be replaced by their acids by point mutations in the expressed sequences or by deamidation of the recombinant structures after expression. Negative charged groups like asparaginic- or glutaminic acid residues should be preferably randomly distributed over the recombinant gelatin-like protein. When desirable an increased number of amino acids with negative charged residual groups can be designed in, as long as this does not result in an increased antigenicity."

on page 9 at lines 8-9:

"In addition it is obvious not to induce marked changes in the basic gelatin structure.";

and on page 11 at lines 5-7:

"In one embodiment the amount of negatively charged groups at pH lower than 8 is increased by deamination of asparagine and/or glutamine to yield aspartic acid and/or glutamic acid.".

Taken together, these statements clearly provide a written description of the practice of the invention and make clear that the invention is limited to those sequences that have the characteristics of collagen or gelatine as we now recited in amended claims 1, 2, 9 and 10.

The Office's objections to the written description appear to relate to the scope of the genus in relation to the disclosed structural species and to an alleged absence of a correlation between function and structure.

Regarding the scope of the genus applicant believes the disclosed structures adequately cover the claimed genus as now defined in amended claims 1, 2, 9 and 10. A sufficient number of representative species is believed described to verify the genus.

In discussing the requirements for the written description on page 7 of the action, the Office references "(if a) biomolecule (is) described only by a functional characteristic". However, that condition does not apply to the present case as the definitions of proteins or protein monomers in applicant's claims all include structural characteristics.

In reaching a conclusion, on page 10 of the action, the Office refers to case law (*In re Wilder*) requiring the specification to describe the invention not an indication of a result that one might achieve if one made the invention. However, this dictum is not at all pertinent to the present case, as will now be explained.

In applicant's claims gelatin-like proteins are recited, with the structural features as now set forth in amended claims 1, 2, 9 and 10, which also have a certain IEP. The IEP is not a result to be achieved but an inherent property of a protein. For a given amino acid sequence, a biochemistry student with basic training can calculate the IEP, for example by reference to the publicly available IEP-calculation program cited on page 14 lines 23-25 of the description. Also the feature of 'having colloid osmotic function' is not a result to be achieved, but is an inherent property of gelatin-like proteins of a certain molecular weight, as is demonstrated by the fact that naturally isolated gelatins were already known to be useful as plasma expanders.

A significant aspect of the invention lies in the finding that a gelatin-like protein with an IEP of less than 8, which applicant believes provides an entirely adequate structural description of the protein as the IEP is an inherent property of a protein, has a low blood clearance rate. It is not clear to what the Office refers in asserting that there is no disclosure of a correlation between function and structure (page 9 of the action). Applicant has found that gelatin-like proteins with an IEP less than 8 have a low blood clearance rate when used in saline as plasma expanders. In light of applicant's disclosure, the art will understand how to make a wide variety of gelatin-like proteins with an IEP less than 8. Since the law does not require the description of an invention to include a disclosure of a mechanism of action, there appears to be no basis for applicant to show why the isoelectric point affects the clearing rate. Nevertheless, one possible explanation is given on page 15 at lines 1-17 of applicant's specification. Furthermore, the correlation between IEP and clearance rate is shown in the examples.

The gist of the Office's arguments on pages 8 and 9 of the action seems to be that no correlation is seen between function and structure. The structural features related to tuning the isoelectric point of a gelatin-like protein have however been clearly identified as set forth above. A particular isoelectric point requires the presence of positively and negatively charged amino acid residues. Some examples of these were

named on page 10 at lines 18-22: glutamine/glutamic acid; asparagine/aspartic acid; lysine and arginine. A person skilled in the art, for example as defined by the examiner, the concept of isoelectric point, and the structural features related to it are common knowledge and will need no further explanation. In light of the directions in the specification you have cited, one of ordinary skill can readily determine, without undue experimentation other proteins than those specifically disclosed which can be employed in the practice of the invention. Thus, for the foregoing good and meaningful reasons, the written description is believed entirely adequate to support amended Claims 1-7, 9-14, 18-22, 24-27 and 31-32.

Moreover, the specification is believed to provide an entirely adequate written description of the subject matter of new claim 33. In this respect, it is believed that the Office is in error in asserting, as it does, on pages 9-10 of the action that the specification lacks examples beyond the particular SEQ ID NOS: 1-4 shown. In addition to the disclosures cited above, the paragraphs at page 7, lines 12-25 and at page 7, line 27 to page 8, line 5, all describe some of the variations that may be made in the structure of the proteins utilized in practicing the invention. The results to be expected from these structural variations are either stated or implicit.

For example, as these paragraphs describe, having at least 5% proline residues avoids undesired 3-D globular domains. Also, a low proportion of proline residues is to be evenly distributed to avoid giving rise to globular domains and stretches of more than 20 amino acids without a proline residue are also undesirable to avoid globular domains.

Furthermore, the Gly-Xaa-Yaa triplets can be separated by one or more amino acids. A protein may have at least 15% proline residues and no stretch of more than 6 triplets without a proline residue. Also, the gelatin-like protein can have 20 or more than 30 consecutive repeats of Gly-Xaa-Yaa triplets.

The skilled worker armed with these directions, and with the guidance the specification gives regarding possible variation of the molecular weight, isoelectric point and other features of the proteins employed in the claimed composition, when contemplating the specific sequences of SEQ ID NOS: 1-4, will readily be able to envisage a wide range of alternative sequences that could be employed in the practice of the invention. There is no need for the sequences themselves to be recited anew. (See Capon v. Eshhar, 76 USPQ2d 1078 (CA FC 2005). Clearly applicant was in possession of the invention claimed in claim 33.

In view of the above amendments and the discussion relating thereto, it is respectfully submitted that the instant application, as amended, is in condition for allowance. Such action is most earnestly solicited. If for any reason the Examiner feels that consultation with Applicant's representative would be helpful in the advancement of the prosecution, they are invited to call the telephone number below for an interview.

Respectfully submitted,

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